

In the Claims

Please add the following new claims 60-111.

60. A method of diagnosing coeliac disease, or susceptibility to coeliac disease, in an individual comprising:

(a) contacting T cells from the individual with an agent selected from

(i) an epitope comprising sequence which is: SEQ ID NO: 1 or SEQ ID NO: 2, or an equivalent sequence from a naturally occurring homologue of the gliadin represented by SEQ ID NO: 3,

(ii) an epitope comprising sequence comprising: SEQ ID NO:1, or an equivalent sequence from a naturally occurring homologue of the gliadin represented by SEQ ID NO:3, which epitope is an isolated oligopeptide derived from a gliadin protein,

(iii) an analogue of (i) or (ii) which is capable of being recognized by a T cell receptor that recognizes (i) or (ii), which in the case of a peptide analogue is not more than 50 amino acids in length, or

(iv) a product comprising two or more agents as defined in (i), (ii) or (iii), and

(b) determining whether the T cells recognize the agent; recognition by the T cells indicating that the individual has, or is susceptible to, coeliac disease.

61. The method according to claim 60 wherein the agent is an analogue (iii) which comprises (i) or (ii) bound to (a) an HLA molecule, or (b) a fragment of an HLA molecule capable of binding (i) or (ii).

62. The method according to claim 61 wherein the HLA molecule or fragment is in a complex comprising four HLA molecules or fragments of HLA molecules.

63. The method according to claim 60, wherein the T cells which are contacted are

in the form of a sample from the individual.

64. The method according to claim 60, wherein the method comprises administering the agent to the skin of an individual and detecting the presence of inflammation at the site of administration, the detection of inflammation indicating that the T cells of the individual recognize the agent.

65. The method according to claim 60, wherein the T cells are not restimulated in antigen specific manner in vitro before the said determining.

66. The method according to claim 60 in which the recognition of the agent by the T cells is determined by detecting the secretion of a cytokine from the T cells.

67. The method according to claim 66 in which the cytokine is IFN- γ .

68. The method according to claim 66 in which the cytokine is detected by allowing the cytokine to bind to an immobilized antibody specific to the cytokine and then detecting the presence of the antibody/cytokine complex.

69. The method according to claim 60 wherein said determining is done by measuring whether the agent binds the T cell receptor.

70. The method for identifying an analogue as defined in claim 60, comprising determining whether a candidate substance is recognized by a T cell receptor that recognizes an epitope comprising sequence as defined in claim 60, recognition of the substance indicating that the substance is an analogue.

71. A method of diagnosing coeliac disease, or susceptibility to coeliac disease, in an individual comprising determining the presence of an antibody that binds to an epitope of an epitope comprising sequence as defined in claim 60 in the individual, the presence of the antibody indicating that the individual has, or is susceptible to, coeliac disease.

72. A method of preventing or treating coeliac disease comprising administering an analogue that binds to an antibody as defined in claim 71.

73. A method of determining whether a composition is capable of causing coeliac

disease comprising determining whether a protein capable of being modified by a transglutaminase to an oligopeptide sequence as defined in claim 60 is present in the composition, the presence of the protein indicating that the composition is capable of causing coeliac disease.

74. The method according to claim 73, wherein the said determining is done by contacting the composition with an antibody specific for the sequence which is capable of being modified to the oligopeptide sequence, binding of the antibody to a protein in the composition indicating the composition is capable of causing coeliac disease.

75. A mutant gliadin protein whose wild-type sequence can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60, but which mutant gliadin protein has been modified in such a way that it does not contain sequence which can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60; or a fragment of such a mutant gliadin protein which is at least 15 amino acids long and which comprises sequence which has been modified in said way.

76. A protein that comprises a sequence which is able to bind to a T cell receptor, which T cell receptor recognizes an agent as defined in claim 60, and which sequence is able to cause antagonism of a T cell that carries such a T cell receptor.

77. A method of identifying an antagonist of a T cell, which T cell recognizes an agent as defined in claim 60, comprising contacting a candidate substance with the T cell and detecting whether the substance causes a decrease in the ability of the T cell to undergo an antigen specific response, the detecting of any such decrease in said ability indicating that the substance is an antagonist.

78. A kit for carrying out a method according to claim 60 comprising an agent as defined in claim 60 and a means to detect the recognition of the peptide by the T cell.

79. The kit according to claim 78 wherein the means to detect recognition comprises an antibody to IFN- γ complex.

80. A kit according to claim 79 wherein the antibody is immobilized on a solid

support and optionally the kit also comprises a means to detect the antibody/IFN- γ complex.

81. An agent as defined in claim 60.

82. An antagonist of a T cell which has a T-cell receptor as defined in claim 60 (iii).

83. A pharmaceutical composition comprising an agent as defined in claim 81 and a pharmaceutically acceptable carrier or diluent.

84. A pharmaceutical composition comprising an antagonist as defined in claim 82 and a pharmaceutically acceptable carrier or diluent.

85. A composition for tolerising an individual to a gliadin protein to suppress the production of a T cell or antibody response to an agent as defined in claim 60, which composition comprises an agent as defined in claim 60.

86. A composition for antagonizing a T cell response to an agent as defined in claim 60, which composition comprises an antagonist of a T-cell which has a T-cell receptor as defined in claim 60 (iii).

87. A method of preventing or treating coeliac disease comprising administering an agent as defined in claim 60, or an antagonist of a T cell which has a T cell receptor as defined in claim 60 (iii).

88. A method of preventing or treating coeliac disease comprising (a) diagnosing coeliac disease in an individual in a method as defined in claim 60, and (b) administering to an individual diagnosed in (a) as having, or being susceptible to, coeliac disease a therapeutic agent for preventing or treating coeliac disease.

89. A mammal that expresses a T cell receptor as defined in claim 60.

90. A method of identifying a product which is therapeutic for coeliac disease comprising administering a candidate substance to a mammal as defined in claim 89 which has, or which is susceptible to, coeliac disease and determining whether the substance prevents or treats coeliac disease in the mammal, the prevention or treatment of coeliac

disease indicating that the substance is a therapeutic product.

91. A method of preventing or treating coeliac disease comprising administering a therapeutic agent identified in the method of claim 90.

92. A polynucleotide that comprises a coding sequence that encodes;

(a) a mutant gliadin protein whose wild-type sequence can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60, but which mutant gliadin protein has been modified in such a way that it does not contain sequence which can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60; or a fragment of such a mutant gliadin protein which is at least 15 amino acids long and which comprises sequence which has been modified in said way or fragment thereof; or

(b) a protein that comprises a sequence which is able to bind to a T cell receptor, which T cell receptor recognizes an agent as defined in claim 60, and which sequence is able to cause antagonism of a T cell that carries such a T cell receptor.

93. The polynucleotide according to claim 92 that additionally comprises one or more regulatory sequences operably linked to the coding sequence, which regulatory sequences are capable of securing the expression of the coding sequence in a cell.

94. The polynucleotide according to claim 93 wherein the regulatory sequence(s) allow expression of the coding sequence in a prokaryotic or mammalian cell.

95. The polynucleotide according to claim 93 which is a vector or which is in the form of a vector.

96. A cell comprising a polynucleotide as defined in claim 92 or which has been transformed with such a polynucleotide.

97. The cell according to claim 96 which is a prokaryotic cell or a mammalian cell.

98. A process for the production of a protein encoded by a coding sequence as defined in claim 92 which process comprises:

(a) cultivating a cell comprising a polynucleotide as defined in claim 92 or which has been transformed with such a polynucleotide wherein such cell is selected from a prokaryotic cell, mammalian cell or is a cell of a graminaceous monocotyledon, under conditions that allow the expression of the protein; and optionally

(b) recovering the expressed protein.

99. A method of obtaining a transgenic plant cell comprising:

(a) transforming a plant cell with a vector according to claim 95 to give a transgenic plant cell.

100. A method of obtaining a first-generation transgenic plant comprising:

(b) regenerating a transgenic plant cell transformed with a vector according to claim 95 to give a transgenic plant.

101. A method of obtaining a transgenic plant seed comprising:

(c) obtaining a transgenic seed from a transgenic plant obtainable to step (b) of claim 100.

102. A method of obtaining a transgenic progeny plant comprising obtaining a second-generation transgenic progeny plant from a first-generation transgenic plant obtainable by a method according to claim 100, and optionally obtaining transgenic plants of one or more further generations from the second generation progeny plant thus obtained.

103. A method according to claim 102 comprising:

(d) obtaining the transgenic seed from the first generation transgenic plant then obtaining a second-generation transgenic progeny plant from the transgenic seed;

and/or

(e) propagating clonally the first-generation transgenic plant to give a second-generation progeny plant;

and/or

(f) crossing the first-generation transgenic plant with another plant to give a second-generation progeny plant;

and optionally

(g) obtaining transgenic progeny plants of one or more further generations from the second-generation progeny plant thus obtained.

104. A transgenic plant cell, plant, plant seed, progeny plant or callus comprising a polynucleotide as defined in claim 92.

105. A transgenic plant cell, plant, plant seed, progeny plant or callus according to claim 104 which is from a graminaceous monocotyledon.

106. A transgenic plant cell, plant, plant seed, progeny plant or callus according to claim 104 which is from wheat, maize, oats, rye, rice, barley, triticale, sorghum or sugar cane.

107. A method of obtaining a crop product comprising harvesting a crop product from a plant according to claim 104 and optionally further processing the harvested product.

108. The method according to claim 107 wherein the plant is a wheat plant and the harvested crop product is grain; optionally further processed into flour or another grain product.

109. A crop product obtainable by a method according to claim 107.

110. A food that comprises a mutant gliadin protein whose wild-type sequence can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60, but which mutant gliadin protein has been modified in such a way that it does not contain sequence which can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60; or a fragment of such a mutant gliadin protein which is at least 15 amino acids long and which comprises sequence which has been modified in said way or a protein that comprises a sequence which is able to bind to a T cell receptor, which T cell receptor recognizes an agent

as defined in claim 60, and which sequence is able to cause antagonism of a T cell that carries such a T cell receptor.

111. The food according to claim 110 in which a mutant gliadin protein whose wild-type sequence can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60, but which mutant gliadin protein has been modified in such a way that it does not contain sequence which can be modified by a transglutaminase to a sequence that comprises an epitope comprising sequence as defined in claim 60; or a fragment of such a mutant gliadin protein which is at least 15 amino acids long and which comprises sequence which has been modified in said way or a protein that comprises a sequence which is able to bind to a T cell receptor, which T cell receptor recognizes an agent as defined in claim 60, and which sequence is able to cause antagonism of a T cell that carries such a T cell receptor is used instead of wild-type gliadin.

Please cancel claims 1-59.